Remarks:

Claims 1, 2, 14-17, 21-23 and 26-30 are pending in the instant application. Each amended claim has written support in the specification; accordingly, no new matter has been added to the application. Reconsideration of the amended claims is respectfully requested.

Written support for amended claims 1, 15, 16 and 28 appears in the specification, for example, at page 4, lines 10-15 and at page 46, lines 4-9.

Written support for amended claim 1 also appears in the specification, for example, at page 5, lines 16-22.

The remaining claim amendments make only formal changes that do not add new matter to the application.

Applicants acknowledge vacation of the previous office action mailed March 10, 2005 and transfer of the instant application to art unit 1656.

Oath/Declaration. Applicants request withdrawal of the rejection of the oath because a newly executed oath by inventor Jose Duca is enclosed. Jose Duca's signature is properly dated in the enclosed oath.

Claim objections. The claim objections are moot because claims 5 and 20 are cancelled.

Claim Rejections Under 35 U.S.C. § 112 (¶2). Claim 25 stands rejected as allegedly indefinite due to the term "SCH549128". The rejection is moot and should be withdrawn because claim 25 has been cancelled.

Claims 26 ands 27 are rejected as allegedly indefinite because the claims refer to coordinates of a crystal and not of a polypeptide. The rejection should be withdrawn because amended claims 26 and 27 refer to coordinates of a polypeptide.

Claim Rejections Under 35 U.S.C. § 101. Claims 1-5 stand rejected as allegedly reading on non-statutory/unpatentable subject matter. Specifically, the Examiner states that the claims include polypeptides that are products of nature and not products of man. The rejection of claims 3-5 is moot since the claims have been cancelled. Applicants request withdrawal of the claim rejections of claims 1 and 2 since the amended claims relate to a "purified" polypeptide which is a product of man.

Claim Rejections Under 35 U.S.C. § 112 (¶1)-written description. Claims 1-3 and 15-33 stand rejected for an alleged lack of written description in the application. The Examiner took the position that the claims cover a genus of polypeptides (claims 1-3, 15-18, 21-25 and 28-32) and crystals (claims 16-33) not sufficiently described by disclosure of an association between polypeptide structure and function. The rejection of claims 3, 18-20, 24, 25 and 31-33 is moot since the claims have been cancelled.

Adequate written description exists if there is sufficient detail provided to convey to a practitioner of ordinary skill in the art that applicants had possession of the claimed invention at the time of filing. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991). Applicants submit that the amended claims are supported by a sufficiently detailed disclosure. Although the claims do not identify the precise amino acid sequence of each claimed polypeptide and of each polypeptide in the claimed crystals, the instant specification provides an abundant amount of detail regarding what polypeptides are acceptable. Certainly, a practitioner of ordinary skill in the art would have readily recognized that applicants had possession of the entire claimed invention.

For example, the specification and the amended claims associate the structure of the recited polypeptide with the function of the polypeptide. Specifically, the amino acid sequence of the HDM2 polypeptide of the amended claims is associated with the ability of the polypeptide to remain soluble at high concentrations (at least 34 mg/ml) and also with the ability of the polypeptide to associate with Ac-$^{6Cl}WAC_{3c}E$, Ac-$^{6Br}WAC_{3c}E$ or p53. The claims and specification provide specific guidance to a practitioner as to which amino acid positions may be modified. The claimed, modified HDM2 polypeptides and the crystals thereof were identified by first locating hydrophobic patches on the surface of the HDM2 3-dimensional structure, then interrupting these patches by replacement of hydrophobic residues with hydrophilic residues (see page 9, line 24 to page 10, line 12). Any of seven positions within the hydrophobic patch can be modified. Moreover, whichever amino acid substitutions that are selected, a certain level of solubility must result for the polypeptide to fall within the claim. Specifically, as mentioned above, the polypeptide must be soluble at high concentrations- at least 34 mg/ml. Furthermore, any modification chosen must not disrupt the HDM2 binding site to such an extent that the molecules Ac-$^{6Cl}WAC_{3c}E$, Ac-$^{6Br}WAC_{3c}E$ or p53 cannot bind.

The specification provides guidance as to which modified polypeptides are acceptable, for example, at table 1 (page 24). In table 1, several acceptable substitutions are set forth. The specification goes on to exemplify four separate polypeptides- SEQ ID NOs: 6, 8, 10 and 12. The specification additionally provides the crystal structure of two acceptable polypeptides in examples 2 and 3.

The Examiner also took the position that the claims lacked sufficient written description because an insufficient number of species of the "genus of claimed polypeptides" have been presented. Applicants submit that, in view of the specification, a practitioner of ordinary skill in the art would have recognized that Applicants had possession of all of the claimed polypeptides and crystals. The specification sets forth four different examples of specific, acceptable polypeptides (SEQ ID NOs: 6, 8, 10, 12) and, as discussed above, provides detailed guidance as to how to select an acceptable polypeptide or crystal. Although the instant claims should be interpreted as broadly as is reasonable and Applicants are *by no means* advocating a restrictive interpretation of the instant claims, the claimed genus is not as expansive as to require additional species to be exemplified in the specification. The modified HDM2 polypeptides set forth in the amended claims have only seven amino acid positions that can be varied; the remaining amino acid positions are not variable. Moreover, the amino acids that can be placed in the variable positions are not unlimited, but, rather, are specifically identified (see Sequence Listing at SEQ ID NO: 4 and Table 1 (page 24, lines 10-11)).

The Examiner took the position that the claims fail to recite "even a single structural feature of the claimed genus of crystals". The Examiner also appeared to take the position that claims relating to crystals *must* recite unit cell dimensions in order to comply with the written description requirement. Applicants disagree. Unit cell dimensions are certainly a useful means by which to describe a particular crystal; however, they are *by no means* the only way by which to comply with the written description requirement. Applicants should *not* be limited to the particular crystals

exemplified in the specification as defined by their unit cell dimensions. This would be an unduly limiting application of the written description requirement and contrary to the case law and Patent Office policy. A practitioner of ordinary skill in the art can recognize possession of a crystal in the absence of unit cell dimensions; for example, the amino acid sequence of a crystallized polypeptide is a highly detailed recitation of the structural features of a claimed crystal and should be sufficient for this purpose. In this case, such a practitioner would have appreciated that applicants had possession of the claimed crystals by recitation of the amino acid sequence as a structural feature. Although issued U.S. patents are not *stare decisis*, there are many examples of granted U.S. claims covering polypeptide crystals in the absence of unit cell dimensions. The Examiner's attention respectfully is directed, for example, to U.S. patent nos. 6,524,589; 6,434,489; 6,153,579; and 5,866,114. Withdrawal of the rejection is requested.

Claim Rejections Under 35 U.S.C. § 112 (¶1)-enablement. Claims 1-3 and 15-33 stand rejected for allegedly lacking a sufficiently enabling disclosure. The examiner takes the position that the scope of claims 1-3, 15-18 and 21-32 is overly broad and not commensurate with the specification. Applicants submit that the amended claims are enabled and that withdrawal of the rejection is warranted. The rejection of claims 3, 18-20, 24, 25 and 31-33 should be withdrawn since the claims have been cancelled.

As the examiner is aware, the fact that *some* experimentation may be required does *not* render a claimed invention unenabled. *In re Colianni*, 561 F.2d 220 (CCPA 1977); *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988). A practitioner of ordinary skill in the art could, using the

specification as a guide, select and synthesize any of the claimed compositions without an undue amount of experimentation. Such an operation could be done using conventional methodologies that are well known in the art.

Specifically, a practitioner could easily choose and express/synthesize a polypeptide sequence set forth in SEQ ID NO: 4 which specifically states the amino acid sequence and acceptable variable positions using conventional molecular biological techniques. The specification provides detailed guidance, in the examples section, regarding the selection, expression and purification of such a polypeptide (see *e.g.*, example 1, starting at page 42). Using no special technical skills or extended experimentation, such a practitioner could test the ability of such a selected polypeptide to remain soluble at 34 mg/ml (or more) and whether such a polypeptide can bind either of the three molecules set forth in the claims. Again, without an undue amount of experimentation, a practitioner could proceed to crystallize such a polypeptide. The specification also provides detailed guidance as to how to crystallize a polypeptide of the invention (see *e.g.*, example 2, starting at page 45; and example 3, starting at page 63). Withdrawal of the rejection is requested.

Claim Rejections Under 35 U.S.C. § 102. Claims 28-31 stand rejected as allegedly anticipated by Schubert *et al.* (US 2004/0197893) and by Kussie *et al.* (Science 274: 948-953 (1996)). The Examiner alleges, in substance, that the cited art discloses crystals comprising a polypeptide that is identical to that of the claimed crystals and that if the crystals in the cited art were compared to the claimed crystals by superimposing conserved backbone atoms, the RMSD value would be about 2.0 Å or less. The rejection of claim 31 is moot since the claim has been cancelled.

Applicants submit that the amended claims are not anticipated by either of Schubert *et al.* or Kussie *et al.* because the claimed crystals are different from that of the cited publications.

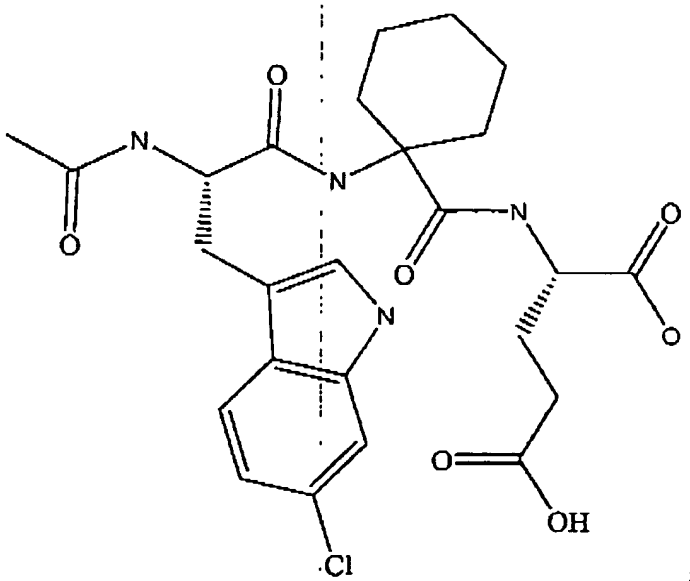
As the Examiner knows, in order to anticipate a claim, a reference must teach each and every element of the claim (see *e.g.*, M.P.E.P. § 2103). As stated by the Federal Circuit:

> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Also,

> The identical invention must be shown in as complete detail as is contained in the ... claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

The cited references fail to meet this standard. Specifically, the claims are directed to a polypeptide that is



complexed with ; in

contrast, neither of the cited references teaches or suggests a polypeptide that is complexed with this molecule. Withdrawal of the claim rejection is requested.

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Conclusion:

Applicants submit that the claims are in condition for passage to allowance. Such action is requested.

Respectfully submitted,

Date: 2/24/2006

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